Newborn Screening Guide

Newborn Screening Guide

Revised 12/15/05

Important News on Expanded Newborn Screening

As most of you are aware, SB 24 was passed in the 2005 Legislative Session to expand the number of conditions for which newborn screening is completed in Kentucky. The complete expansion will be effective December 31, 2005, and at that time a total of 29 conditions will be included on the screen which puts Kentucky in line with the national recommendation from the March of Dimes. Changes began in the newborn screening process effective July 2005 and the bullets below highlight important information for submitters of newborn screens and hospitals.

For All Submitters of Newborn Screens, including Hospitals:

- The new technology will detect disorders at 24 hours of age. The optimal specimen should be collected at 24 hours of age, but no later than 48 hours of age.
- If the infant is going to receive a blood transfusion, if possible, get the blood spot specimen prior to giving the transfusion even if the infant is not 24 hours of age.
- Antibiotics need to be documented on the filter paper card but will not automatically require a repeat.
- Demographic information and physician of record should be verified with the parent on the specimen to ensure that the physician and family can be contacted quickly in the situation of a positive screen.
- The specimen needs to be mailed to the state lab within 24 hours of collection, so the mail process at the submitting facility should examine their mailing procedure to assure entry into the USPS (United States Postal Service) as soon as possible after collection.
- There will be an educational presentation available on https://ky.train.org

Specific to Hospitals:

- Hospitals are required to have a newborn screening coordinator designated with the Department for Public Health Newborn Screening Program on an annual basis in January. Newborn Nursery nurse managers will be contacted to provide information.
- Hospitals will be required to implement a protocol to assure all newborns receive a newborn screening blood test and submit to the Department for Public Health.
- Hospitals will also be required to provide educational information to parents regarding newborn screening. This information is available on the HRSA website http://mchb.hrsa.gov/programs/default.htm and scroll down to Newborn Screening brochure.

Follow-Up:

Short Term follow-up for abnormal or unsatisfactory specimens is conducted by state staff at the Department for Public Health.

Abnormal Result

- The state lab notifies the follow-up staff of the abnormal result.
- The follow-up staff contacts the primary care physician listed on the NBS filter paper card by telephone with further action and faxes information to their office.
- The Department for Public Health contracts with University of Kentucky and the University of Louisville for specialty clinic referrals.

Unsatisfactory Specimen

- The laboratory staff mails out results either with a letter explaining to repeat only one test or if no letter is attached, the entire specimen needs to be repeated.
- If a repeat specimen is not received within 10 days, a letter is mailed to the parent explaining that no repeat has been received and to contact their baby's PCP.

After analyzing the data on the T4 levels the new cut off value will be 5.0ug/dL effective December 5, 2005. We will continue to monitor this and may adjust further in the future.

Disorders included in the screen as of December 31, 2005 are:

Disorders of Amino Acid Metabolism:

1. Phenylketonuria (PKU)
2. Maple Syrup Urine Disease (MSUD)
3. Homocystinuria (HCY)
4. Citrullinemia (CIT)
5. Arginosuccinic acidemia (ASA)
6. Tyrosinemia type 1 (TYR 1)

Disorders of Fatty Acid Oxidation

7. Medium chain acyl-CoA dehydrogenase deficiency (MCAD)
8. Very long chain acyl-CoA dehydrogenase deficiency (VLCAD)
9. Long-chain hydroxyacyl-CoA dehydrogenase deficiency (LCHAD)
10. Short-chain acyl-CoA dehydrogenase deficiency (SCAD)
11. Trifunctional protein deficiency (TFP)
12. Carnitine uptake defect (CUD)

Disorders of Organic Acid Metabolism

13. Isovaleric acidemia (IVA)
14. Glutaric acidemia type 1 (GA 1)
15. 3-hydroxy-3-methyl glutaric aciduria (HMG)
16. Multiple carboxylase deficiency (MCD)
17. Methylmalonic acidemia (Cbl A, B)
18. Methylmalonic acidemia mutase deficiency (MUT)
19. Propionic Acidemia (PA)
20. β-ketothiolase deficiency (BKT)
21. 3-Methylcrotonyl-CoA carboxylase deficiency

Hemoglobinopathies

22. Sickle Cell Disease
23. Hemoglobin SC Disease
24. Hemoglobin S/β-thalassemia

Others

25. Galactosemia
26. Biotinidase deficiency
27. Congenital Adrenal Hyperplasia (CAH)
28. Cystic Fibrosis (CF)
29. Congenital Hypothyroidism (CH)

For more information contact Sandy Fawbush at 502-564-3756 Ext 3761 or sandy.fawbush@ky.gov

Insert copy of your hospital protocol and submit a copy of protocol and the complete the contact information sheet for the Newborn Screening Coordinator at your facility and mail to:

Department for Public Health
Newborn Screening Program
275 East Main St HS 2GW-C
Frankfort, KY 40621

Newborn Screening Coordinator Information

Facility Name _____

Coordinator Name _____

Telephone Number _____

Email _____

Completed by:

_____ _____
Name Title

Please complete and fax to the Newborn Screening Program 502-564-1510.

PROPER SPECIMEN COLLECTION PROCEDURE

The filter paper forms should be stored in a cool, dry place. Be sure to take note of the form expiration date printed on the filter paper margin below the circles. The filter paper forms are to be used on or before the expiration date. Destroy all outdated forms immediately and request a new supply from the Kentucky Public Health Laboratory. Order no more forms than can be used in 6 months.

Gloves should be worn for personal safety. Care should be taken to avoid contamination of blood collection circles with antiseptic solutions, powders, lotions or other materials, which may adversely affect the testing process.

1. When collecting blood, fold back the cover sheet to expose the filter paper. Do not touch or handle the filter paper before or after applying blood.

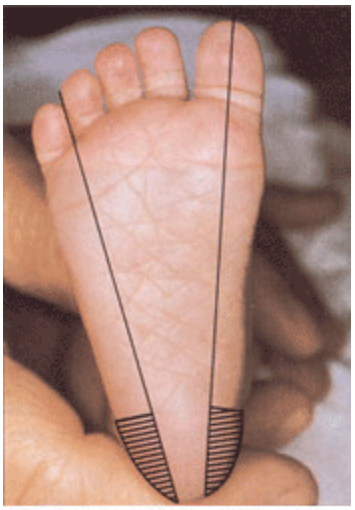
2. Position the infant with feet lowered below the heart to help to increase the blood flow.

3. Warm the heel to increase the blood flow to the area by covering the puncture site for three to five minutes with a warm, moist towel which has been run under tap water at a temperature of not more than 42 degrees centigrade or 107.6 degrees F.

4. Clean the puncture site with a sterile alcohol pad. Allow to air dry. Excess alcohol may cause hemolysis and denature some of the enzymes tested.

5. Use a sterile disposable lancet with a 2.0 mm tip or an automatic lancet to perform a swift clean puncture in the areas indicated on the diagram. Wipe away the first drop of blood with dry sterile gauze.

   Recommendation for Heel Puncture Site in Newborns:
   Perform punctures on the most lateral portions of the plantar surface (in the hatched portion of the foot in the photo to the right).



Hatched area (▨) indicates safe areas for puncture site.

6. Allow a large drop of blood to form. To enhance blood flow during collection, very gentle intermittent pressure may be applied to the area surrounding the puncture site. Excessive "milking" causes an admixture of tissue fluids with the blood specimen, resulting in an unsatisfactory specimen.

7. Do not use a capillary tube. Lightly touch the filter paper against a large drop of blood and allow a sufficient quantity of blood to soak through to completely fill the circle. Apply blood to one side of the filter paper only, allowing full saturation of each circle area. Either side may be chosen for this procedure. Fill all circle areas. Do not layer successive small drops of blood to the same circle. Avoid touching or smearing the blood spots.

8. If blood flow is diminished, repeat steps three through six with sterile equipment.

9. Special Considerations: Do not draw from intravenous lines where TPN or blood is being infused. For other types of IV fluids, make sure the line has been thoroughly flushed before attempting specimen collection. Avoid syringes with additives. Draw 2 to 2.5 cc from the line before sample is obtained. Spot the card immediately after specimen collection.

10. Allow the blood specimens to air-dry for at least 3 hours on a flat, nonabsorbent surface protected from heat or direct sunlight. Do not refrigerate the samples.

11. Ship collection forms to the Kentucky Public Health Laboratory after at least 3 hours drying time. Remember to **"Draw, Dry, and Drop (in the mail)."** Do not accumulate or "batch" specimens before shipping since this may result in specimens too old to test. When placing more than one specimen in an envelope, alternate orientation of collection forms so that blood spots on adjacent forms are not in contact. Delayed submission to the laboratory may result in significant delay in identification of an infant with a disorder.

12. After completing the form and collecting the specimen, ship to: Department for Public Health, Division of Laboratory Services, P. O. Box 2010, Frankfort, KY 40602.

The Kentucky Public Health Laboratory assumes responsibility for testing only; whoever submits specimens must assume liability for proper identification, collection and prompt delivery of specimens to the State Lab.

Neonatal Screening Blood Specimen Collection and Handling Procedure

1

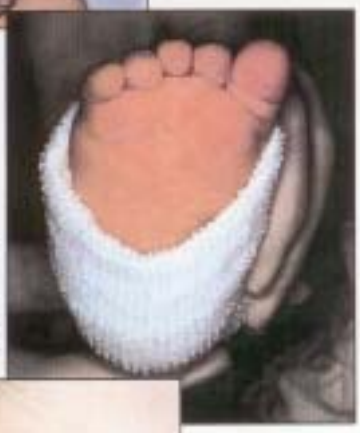
Equipment: Sterile lancet with tip approximately 2.0 mm, sterile alcohol prep, sterile gauze pads, soft cloth, blood form, gloves.

2

Complete ALL information. Do not contaminate filter paper circles by allowing the circles to come in contact with spillage or by touching before or after blood collection. Keep "SUBMITTER COPY" if applicable.

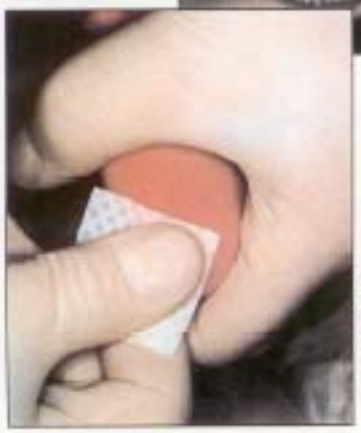
3

Hatched area ( ) indicates safe areas for puncture site.



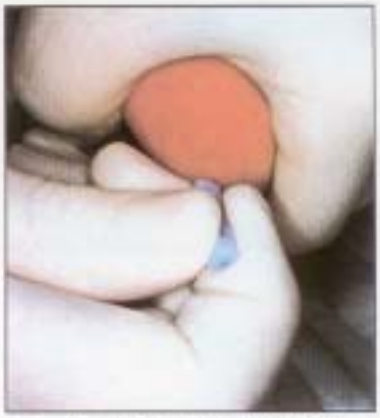
4

Warm site with soft cloth, moistened with warm water up to 41°C, for three to five minutes.



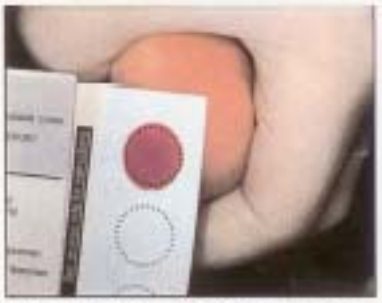
5

Cleanse site with alcohol prep. Wipe DRY with sterile gauze pad.



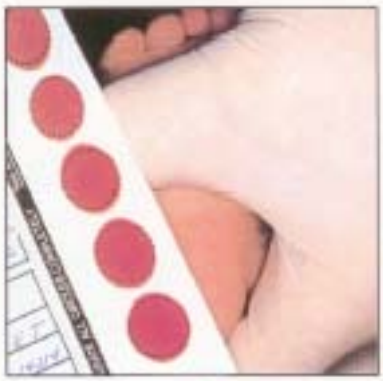
6

Puncture heel. Wipe away first blood drop with sterile gauze pad. Allow another LARGE blood drop to form.



7

Lightly touch filter paper to LARGE blood drop. Allow blood to soak through and completely fill circle with SINGLE application to LARGE blood drop. (To enhance blood flow, VERY GENTLE intermittent pressure may be applied to area surrounding puncture site.) Apply blood to one side of filter paper only.



8

Fill remaining circles in same manner as step 7, with successive blood drops. If blood flow is diminished, repeat steps 5 through 7. Care of skin puncture site should be consistent with your institution's procedures.

9

Dry blood spots on a dry, clean, flat, non-absorbent surface for a minimum of four hours.

10

Mail completed form to testing laboratory within 24 hours of collection.

Information provided by New York State Department of Health

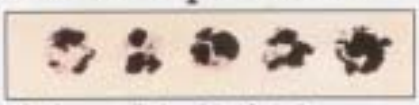
Simple Spot Check

Valid Specimen

Allow a sufficient quantity of blood to soak through to completely fill the preprinted circle on the filter paper. Fill all required circles with blood. Do not layer successive drops of blood or apply blood more than once in the same collection circle. Avoid touching or smearing spots.

Invalid Specimens

Possible Causes



1. Specimen quantity insufficient for testing.

- Removing filter paper before blood has completely filled circle or before blood has soaked through to second side.
- Applying blood to filter paper with a capillary tube.
- Touching filter paper before or after blood specimen collection with gloved or ungloved hands, hand lotion, etc.
- Allowing filter paper to come in contact with gloved or ungloved hands or substances such as hand lotion or powder, either before or after blood specimen collection.

2. Specimen appears scratched or abraded.

- Applying blood with a capillary tube or other device.

3. Specimen not dry before mailing.

- Mailing specimen before drying for a minimum of four hours.

4. Specimen appears supersaturated.

- Applying excess blood to filter paper, usually with a device.
- Applying blood to both sides of filter paper.

5. Specimen appears diluted, discolored or contaminated.

- Squeezing or "milking" of area surrounding the puncture site.
- Allowing filter paper to come in contact with gloved or ungloved hands, or substances such as alcohol, formula, antiseptic solutions, water, hand lotion or powder, etc., either before or after blood specimen collection.
- Exposing blood spots to direct heat.

6. Specimen exhibits serum rings.

- Not wiping alcohol from puncture site before making skin puncture.
- Allowing filter paper to come in contact with alcohol, hand lotion, etc.
- Squeezing area surrounding puncture site excessively.
- Drying specimen improperly.
- Applying blood to filter paper with a capillary tube.

7. Specimen appears clotted or layered.

- Touching the same circle on filter paper to blood drop several times.
- Filling circle on both sides of filter paper.

8. No blood.

- Failure to obtain blood specimen.

Schleicher & Schuell

Schleicher & Schuell, Inc. • 10 Optical Avenue • Keene, NH 03431

Manufacturer of 903 Specimen Collection Paper

Information provided by New York State Department of Health

There may be other tests besides those required in your state. More helpful information is available by contacting:

The National Newborn Screening and Genetics Resource Center

(512) 454-6419

www.genes-r-us.uthscsa.edu

or

Kentucky's Newborn Screening Program

(502) 564-3756 ext. 3761

http://chfs.ky.gov/dph/ach/newbornscreening.htm

U.S. Department of Health and Human Services
HRSA
Health Resources and Services Administration

These Tests Could Save Your Baby's Life

Newborn Screening Tests

Why does my baby need Newborn Screening tests?

Most babies are healthy when they are born.

We test all babies because a few babies look healthy but have a rare health problem.

If we find problems early, we can help prevent serious problems like mental retardation or death.

How will my baby be tested?

Before you leave the hospital, a nurse will take a few drops of blood from your baby's heel. The hospital will send the blood sample to a newborn screening lab.

How will I get the results of the test?

Parents are notified of test results if there is a problem.

Ask about results when you see your baby's health professional.

Why do some babies need to be retested?

Your baby may be retested if you leave the hospital before 24 hours.

Some States require a second test on all babies.

Some babies need to be retested because there is a problem with the blood sample.

A few babies need to be retested because the first test showed a possible health problem.

What if my baby needs to be retested?

Your baby's health professional or the State Health Department will contact you if your baby needs to be retested. They will tell you why the baby needs to be retested and what to do next.

If your baby needs to be retested, get it done right away.

Make sure that your hospital and health professional have your correct address and phone number.

What if I have questions?

Ask your baby's health professional if you have questions or concerns.

Qué puedo hacer si tengo preguntas?

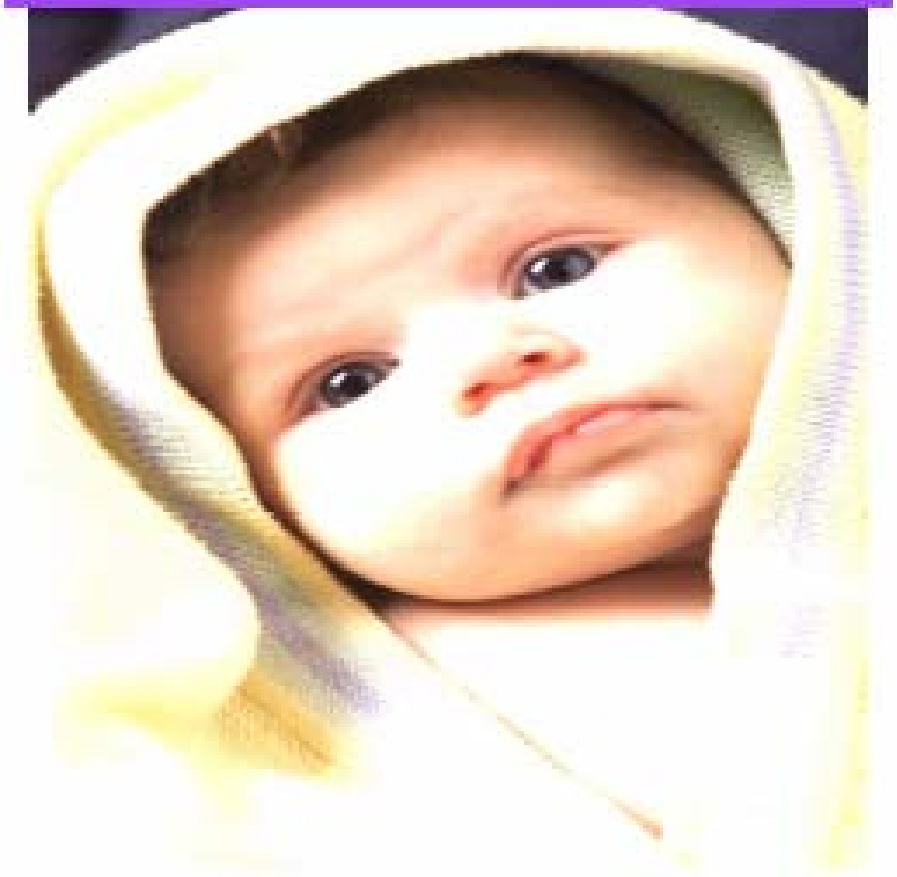
Si tiene preguntas o dudas, hable con el professional medico de su bebé.

Es posivle que haya preubas adicionales quie el departmento de salud de su estado no require. Para mas informacion en ingles, pongase en contacto con:

The National Newborn Screening and
Genetics Resource Center
(512) 454-6419
www.genes-r-us.uthscsa.edu
Or
Llame al porgrama de su estado
Kentucky's Newborn Screening Program
(502) 564-3756 ext. 3761
http://chfs.ky.gov/dph/ach/newbornscreening.htm

Esta Prueba Puede Slavar la Vida de su Bebé

Newborn Screening Tests



¿Por qué mi bebé necesita esta prueb a de sangre?

La mayoría de los bebés nacen sanos.

Le hacemos esta prueb a a todos los bebés porque a veces hay bebés que parecen sanos pero tienen un problema de salud raro.

?Cómo se hace la prueba?

Antes de que le den de alta a su bebé, un enfermero tomará unas gotas de sangre del talón de su bebé.

El hospital enviará la muestra de sangre a un laboratorio especializado.

¿Cómo obtendré los resultados de la prueba?

Si hay algún problema, usted será notificado de los resultados lo más antes posible.

Todos los resultados se envían al profesional médico de su bebé.

¿Por qué algunos bebé necesitan más pruebas?

Si le dan de alta a su bebé antes de las 24 horas, es posible que haya que repetir la prueba.

En algunos estados, todos los bebés recib en dos pruebas.

A veces se necesita otra muestra de sangre porque hubo problemas con la primera.

Otras veces se necesita otra muestra de sangre porque la primera mostró la posibilidad de un problema de salud.

¿Y si mi bebé necesita otra prueba?

Si su bebé necesita que se repita la prue ba, el profesional médico de su bebé o el departamento de salud del estado se pondrán en contacto con usted. Ellos le dirán por qué su bebé necesita otra prueba y lo que usted tiene que hacer.

Asegúrese que el hospital y su professional médico tengan su número de teléfono y dirección.

ERNIE FLETCHER
GOVERNOR

CABINET FOR HEALTH AND FAMILY SERVICES
DEPARTMENT FOR PUBLIC HEALTH
DIVISION OF
ADULT AND CHILD HEALTH IMPROVEMENT
275 EAST MAIN STREET, HS2W-C
FRANKFORT, KENTUCKY 40621
(502) 564-3756, (502) 564-1510 FAX

Mark D. Birdwhistell
Secretary

Laboratory Contact Information

YOU SHOULD RECEIVE AND OFFICIAL COPY OF THE NEWBORN SCREENING LAB RESULTS BUT SHOULD YOU NEED A COPY PLEASE FAX COMPLETED REQUEST FORM TO THE NUMBER BELOW:

FAX REQUEST FOR RESULTS: FAX # 502-564-2905

A COPY OF REQUEST FORM TO BE COMPLETED INCLUDED IN THIS BINDER.

TO ORDER SPECIMEN COLLECTION FORMS: 502-564-4446 EXT 4440

LABORATORY STAFF: 502-564-4446 EXT. 4434

Short Term Follow-Up (prior to university referral) Contact Information

Sandy Fawbush, RN: Phone: 502-564-3756 Ext. 3761
Troi Cunningham, RN 800-462-6122 Ext. 3761
Mary Sue Flora, RN sandy.fawbush@ky.gov

Newborn Screening Program Fax: 502-564-1510

PROVIDER FAX REQUEST
FOR LABORATORY INFORMATION

Date: _____

Please verify that all information below is completed accurately and legibly. We also request that you include a telephone number where you can be reached in the event we have questions and a fax number so you can receive the information you've requested. Thank you.

Infant Name: _____DOB: _____Sex: _____

Mother's Name: _____

Mother's SSN: _____

Requested Lab Values:_____

_____

Who is making this request?

PCP Name: _____

PCP Phone: (_____)_____

PCP Fax # (so request can be processed): _____

PCP Address: _____

_____

Newborn Screening Program

Resources for Metabolic Disorders

Amino Acid Disorders, Organic Acid and Fatty Acid Disorders

Clinic	Staff	Phone
University of Kentucky Lexington, KY **Primary Contact Number** **(859) 323-5404** Primary Contact Carol Reid MT (ASCP), MPA **Emergency after hours:** **(800) 888-5533** **(Page metabolic/newborn screening physician)**	Carol Reid, MT (ASCP), MPA C. Charlton Mabry, MD Carolyn Bay, MD Fax:(859) 323-8179	(859) 323-5404 (859) 323-5404 (859) 257-5559
University of Louisville Louisville, KY (502) 852-3879 **Primary Contact Number** **(502) 852-5334** **Emergency after hours: (502) 562-9914 beeper**	Joseph Hersh, MD MD After hours pager # Gordon Gowans, Alexander Asamoah, MD Karen Kinkus, RD Fax: (502) 852-7886	(502) 852-5334 (502) 562-9914 (502) 852-3879

Newborn Screening Program

Resources for Cystic Fibrosis

Clinic	Staff	Phone
University of Kentucky Division of Pediatric Pulmonology Carol Reid MT (ASCP), MPA **(859) 323-5404** **Emergency after hour:** **(800) 888-5533 (ask for pediatric pulmonology on call)**	Carol Reid, MT, (ASCP), MPA Michael Anstead, MD Jamshed F. Kanga, MD Fax: (859) 257-1888	(859) 323-5404 (859) 257-5536
University of Louisville Pediatric Pulmonary Medicine **(502) 629-8830** **Emergency after hours: (502) 629-6000** **(Page pediatric pulmonology)**	Martha Eddy, CPNP Ronald Morton, MD Nehm Eid, MD Fax: (502) 629-7540	(502) 629-8830 (502) 629-8830

Newborn Screening Program
Resources for Endocrinology

(Congenital Adrenal Hyperplasia, Congenital Hypothyroidism)

Clinic	Staff	Phone
University of Kentucky **(859) 323-5404** Dept. of Pediatrics Endocrinology and Metabolism Carol Reid MT, (ASCP), MPA **Emergency after hours: (800) 888-5533** **(ask for Pediatric Endocrinology)**	Carol Reid MT, (ASCP), MPA Jeff Lomenick, MD Jackson Smith, MD Fax: (859) 323-8179	(859) 323-5404 (859) 323-5404
University of Louisville **(502) 629-8821** Pediatric Endocrinology **Emergency after hours: 502-629-6000 or** **(800) 292-2759** **(Page pediatric endocrinology)**	Lee Ann Tincher, RN Michael Foster, MD Aaron Davis, MD Kellie Woodruff, ARNP Fax: (502) 629-8824	(502) 629-8821 (502) 629-8821

Newborn Screening Program

Resources for Hemoglobinopathies

(Hb S/S, Hb S/A, Hb S/C)

Clinic	Staff	Phone
University of Kentucky **Pediatric Hematology/Oncology** **Phone: (859) 323-8075** **Emergency after hours: (800) 888-5533** **(ask for pediatric hematology)**	Lisa Hess, ARNP Jeff Moscow, MD Fax: (859) 257-8978	(859) 323-8075 (859) 323-0239
University of Louisville **Pediatric Hematology/Oncology** **Phone (502) 629-7750** **Emergency after hours: (502) 629-6000** **(Page pediatric hematology)**	Diane Burnett, PNP Salvatore Bertelone, MD Fax: (502) 629-7784	(502) 629-7750 (502) 629-7750

Newborn Screening Program

Resources for Newborn Hearing and Screening

Location	Clinic	Consultant	Phone
Louisville, KY (877) 757-4327	Commission for Children with Special Health Care Needs 982 Eastern Parkway Louisville, KY 40217 (877) 757-4327	Karen Mercer, RN Michelle King (877) 757-4327 (HEAR) Ext. 258 (800) 232-1160 Ext. 323	
Central Region (800) 232-1160	Commission for Children with Special Health Care Needs 982 Eastern Parkway Louisville, KY 40217 (800) 232-1160	Eric Cahill (800) 232-1160 Ext. 322	
East Region (800) 817-3874	Commission for Children with Special Health Care Needs 333 Waller Ave. Ste 300 Lexington, KY 40504 (800) 817-3874	Lou Ann Jones (800) 817-3874 Ext. 225 Fax: (859) 225-7155	
West Region (800) 727-9903	Commission for Children with Special Health Care Needs 712 West 15th St. Hopkinsville, KY 42240 (800) 727-9903	Carolyn Kisler (800) 727-9903 Fax: (270) 889-6050	

DISORDERS

Test name	Test Abbreviation	Category
3-methylcrotonyl CoA Carboxylase deficiency	3MCC	Organic Acid Disorders
Argininosuccinic Acidemia	ASA	Amino Acid Disorders
Beta ketothiolase deficiency	BKT	Organic Acid Disorders
Biotinidase Deficiency	BIO	Other
Carnitine uptake defect	CUD	Fatty Acid Oxidation
Citrullinemia	CIT	Amino Acid Disorders
Congenital Adrenal Hyperplasia	CAH	Endocrine
Congenital Hypothyroidism	CH	Endocrine
Cystic Fibrosis	CF	Other
Galactosemia	GALT	Other
Glutaric acidemia type 1	GA-1	Organic Acid Disorders
Hemoglobin S-βeta thalassemia	Hb S/Th	Hemoglobin
Hemoglobin S/C disease	Hb S/C	Hemoglobin
Homocystinuria	HCY	Amino Acid Disorders
Hydroxymethylglutaric aciduria (3-OH 3-CH3 glutaric aciduria)	HMG	Organic Acid Disorders
Isovaleric acidemia	IVA	Organic Acid Disorders
Long-chain L-3hydroxyacyl-CoA dehydrogenase	LCHAD	Fatty Acid Oxidation
Maple Syrup Urine Disease	MSUD	Amino Acid Disorders
Medium-chain acyl-CoA dehydrogenase deficiency	MCAD	Fatty Acid Oxidation
Methylmalonic acidemia	Cbl A, B	Organic Acid Disorders
Methylmalonic acidemia mutase deficiency	MUT	Organic Acid Disorders
Multiple carboxylase deficiency	MCD	Organic Acid Disorders
Phenylketonuria	PKU	Amino Acid Disorders
Propionic Acidemia	PA	Organic Acid Disorders
Short-chain acyl-CoA dehydrogenase deficiency	SCAD	Fatty Acid Oxidation
Sickle cell disease	HB S/S	Hemoglobin
Trifunctional protein deficiency	TFP	Fatty Acid Oxidation
Tyrosinemia type I	TYR I	Amino Acid Disorders
Very long-chain acyl-CoA dehydrogenase deficiency	VLCAD	Fatty Acid Oxidation

Health Care Provider Fact Sheets

Disease Name — 3-methylcrotonyl-CoA carboxylase deficiency

Alternate name(s)	3-methylcrotonylglycinuria
Acronym	3-MCC
Disease Classification	Organic Acid Disorder
Variants	Late-onset form
Variant name	Late-onset 3-methylcrotonyl-CoA carboxylase deficiency
Symptom onset	Many individuals remain asymptomatic into adulthood. Others present in late infancy (generally after 3 months).
Symptoms	Infants can present with a Reye-like syndrome of ketoacidosis, hypoglycemia, hyperammonemia which can lead to seizures, coma and possibly death. Others present with failure to thrive, hypotonia or spasticity. Late-onset 3-MCC may present as developmental delay without Reye-like syndrome. Symptomatic adults often report general weakness and fatigue. Many individuals are asymptomatic.
Natural history without treatment	Primary manifestations appear to be muscular hypotonia and atrophy. Individuals with Reye-like illnesses may die or suffer neurologic insult during these episodes.
Natural history with treatment	Once over the initial crisis, most individuals have been intellectually normal. It is uncertain whether treatment modifies disease course.
Treatment	Protein restricted diet. Leucine-free medical foods. Possible carnitine supplementation. Giving treatment to asymptomatic individuals is of questionable value.
Other	Newborn screening has led to the diagnosis of asymptomatic women whose infants have transiently elevated isovalerylcarnitine.
Physical phenotype	None
Inheritance	Autosomal recessive
General population incidence	1:50,000
Ethnic differences	No known population at increased risk
Population	N/A
Ethnic incidence	N/A
Enzyme location	Inner membrane of the mitochondria, liver and kidney.
Enzyme Function	Breakdown of leucine
Missing Enzyme	3-methylcrotonyl-CoA carboxylase
Metabolite changes	Increased 3-hydroxyisovaleric acid, increased 3-methylcrotonylglycine.
Gene	MCCA/MCCB
Gene location	3q25-q27, 5q12-q13.1
DNA testing available	Sequencing available internationally
DNA testing detail	No common mutations
Prenatal testing	May be possible for at-risk pregnancies using enzymatic analysis.
MS/MS Profile	C5:1 (tigyl or 3-methylcrotonyl carnitine) elevated C5-OH (3-hydroxy-2-methylbutyryl carnitine)- elevated
OMIM Link	www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=210200
Genetests Link	www.genetests.org
Support Group	Organic Acidemia Association www.oaanews.org Save Babies through Screening Foundation www.savebabies.org Genetic Alliance www.geneticalliance.org